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# **Abnormal Uterine Bleeding (including PALM COEIN Classification)**

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**ABSTRACT (no more than 150 words)**

Abnormal uterine bleeding (AUB) is a common and chronic condition, affecting women throughout their reproductive years. The FIGO PALM-COEIN classification system, facilitates understanding of possible AUB aetiology, and allows for characterisation of cause by use of universal terminology to describe menstrual disorders. There are a wide variety of medical and surgical (excisional and non-excisional) treatments available, but often women will choose a period of observation (conservative treatment), after sinister pathology is excluded. Management of AUB has to be tailored to the individual patient as the ultimate of goal is improvement in quality of life.

**KEY WORDS**

Heavy Menstrual Bleeding (HMB)

Abnormal Uterine Bleeding (AUB)

PALM-COEIN

Menstruation

Fibroids

Selective Progesterone Receptor Modulators (SPRMs)

## **DEFINITIONS**

To understand abnormal uterine bleeding (AUB), we must first understand the variances of a normal menstrual cycle. A “normal” menstrual cycle is defined based on four parameters (frequency, regularity, duration, or volume) summarised in Table 1. The National Institute for Care and Excellence (NICE) recommends that heavy menstrual bleeding (HMB), a sub-category of AUB should be recognised based on the impact it has on the woman’s quality of life (QoL), and all interventions must focus on improving QoL, rather than an objective blood loss measurement.

*[Insert Table 1]*

## **MENSTRUAL TERMINOLOGY AND THE NEED FOR A CLASSIFICATION SYSTEM – FIGO PALM COEIN SYSTEM**

The varied use of terminology to describe AUB symptoms has led to difficulties in many areas, including documenting symptoms; determining best medical and surgical treatments; design and interpretation of research data; and attempts to conduct multinational clinical trials.

These concerns were addressed by the Menstrual Disorders Working Group within the International Federation of Gynecology and Obstetrics (FIGO), which subsequently became a standing committee, the Menstrual Disorders Committee (MDC). The FIGO MDC was responsible for the menstrual terminology encouraged for use in clinical care and research today. In addition, the FIGO MDC also developed the PALM-COEIN acronym for subclassifying AUB aetiology. Both FIGO systems have recently been further refined.

## **ABNORMAL UTERINE BLEEDING (AUB)**

AUB was re-defined by (FIGO) in 2009 to introduce standardisation of nomenclature and identify an aetiological basis for AUB in the reproductive years. AUB is the overarching term used to describe any symptomatic variation from normal menstruation (in terms of frequency, regularity, duration, or volume) and also includes intermenstrual bleeding. Table 2 summarises the recommended terminology for women with AUB.

*[Insert Table 2]*

### **Acute AUB**

An episode of uterine bleeding in a woman of reproductive age, who is not pregnant, that is of sufficient quantity to require immediate intervention to prevent further blood loss.

### **Chronic AUB**

Bleeding from the uterine body (or corpus), that is abnormal in frequency, regularity, duration, and/or volume, and has been present for at least the majority of the past six months.

### **Intermenstrual bleeding**

When AUB occurs between well-defined cyclical menses, the symptom is called intermenstrual bleeding (IMB). This symptom may be virtually impossible to discern if the woman has irregular and/or very frequent menses.

These may be further sub divided as

- Cyclic Midcycle IMB – Small quantity of frank vaginal bleeding or discharge around midcycle, corresponding with ovulation due to a nadir in the oestradiol levels, is physiological, and is observed in 9% of women.

- Cyclic Pre or Postmenstrual IMB — Cyclical IMB that predictably occurs either early in the cycle (follicular phase) or late (luteal phase), and typically presents as very light vaginal bleeding for one or more days.
- Acyclic IMB — When the IMB is not cyclical or predictable.

### **Heavy Menstrual Bleeding (HMB)**

Heavy menstrual bleeding (HMB) is a sub-category of AUB and has a woman-centred approach to diagnosis. Rather than using objective measurements of volume, traditionally defined as > 80 mL/cycle using the alkalim-hematin method or using PBAC (Pictorial Blood Assessment Chart) scores, NICE defines HMB as excessive menstrual blood loss (MBL) that interferes with the physical, social, emotional and/or material quality of life. Some authors have found a good correlation between subjective and actual blood loss but not others. A summary of terms that should no longer be used to describe menstrual bleeding patterns is listed in Table 3.

*[Insert Table 3]*

## **DEMOGRAPHICS**

AUB is a common and frequently debilitating condition for women worldwide. It has clinical implications and a high cost for the healthcare system. Uterine fibroids, a common cause of AUB are estimated to cost the US \$5.9 to \$34.4 billion annually. AUB affects 14-25% of women in the reproductive age group resulting in a large proportion of GP referrals within the NHS. A recent HMB audit by the Royal College of Obstetricians and Gynaecologists (RCOG), assessing patient outcomes and experiences in England and Wales, reported that 1-year post referral, only 30% of women (including those managed with surgery) were ‘satisfied’ (or better) at the prospect of current menstrual symptoms

continuing, as currently experienced, for the next five years. Thus, menstrual problems represent a clinical area of unmet need.

## **PALM-COEIN CLASSIFICATION OF AUB**

There are 9 main categories, **P**olyp; **A**denomyosis; **L**eiomyoma; **M**alignancy and **H**yperplasia; **C**oagulopathy; **O**vulatory dysfunction; **E**ndometrial; **I**atrogenic; and **N**ot otherwise classified. In general, the components of the PALM group are discrete (structural) entities that may be identified visually with imaging techniques and/or histopathology, whereas the COEIN group is related to entities that are not defined by imaging or histopathology (non-structural).

The term “DUB”, which was previously used as a diagnosis when there was no systemic or locally definable structural cause for AUB, should be abandoned. These women generally have one or a combination of coagulopathy, a disorder of ovulation, or primary endometrial disorder—the last of which is most often a primary or secondary disturbance in local endometrial haemostasis.

### **Polyps (AUB-P)**

Endometrial polyps are epithelial proliferations arising from the endometrial stroma and glands. The majority are asymptomatic. The reported prevalence of endometrial polyps varies widely depending on the definition of a polyp, the diagnostic method used, and the population studied. Polyps may be endometrial or endocervical.

### **Adenomyosis and AUB (AUB-A)**

Adenomyosis is defined as the presence of ectopic endometrial glands and stroma in the myometrium, although it remains a poorly understood entity. The prevalence of adenomyosis is difficult to ascertain because of a wide variation in diagnostic criteria both with imaging modalities and with histology. It has been estimated that histological confirmation of adenomyosis ranges from 5-70% of patients who undergo hysterectomy.

### **Leiomyomas and AUB (AUB-L)**

Uterine fibroids (myomas, leiomyomas) are the most common benign tumours in women of reproductive age and present in almost 80% of all women by the age of 50. The association between AUB and fibroids is complex and poorly understood, as women with fibroids may be asymptomatic. There is a correlation between AUB and the degree of distortion and penetration of the uterine cavity associated with the fibroid(s). Submucous fibroids are considered to be most commonly associated with AUB/HMB.

### **Malignancy and hyperplasia (AUB-M)**

Endometrial hyperplasia and malignancy are important potential causes of AUB and must be considered in nearly all women of reproductive age. Once identified, the pathology should be further sub-classified using the appropriate WHO or FIGO system. In the UK, endometrial cancer is the fourth most common cancer in women. Historically, endometrial cancer has rarely occurred in premenopausal women; however, with increasing obesity and rising prevalence of the metabolic syndrome, the endocrine-driven subset of endometrial malignancy has markedly increased in frequency.



### **Coagulopathy (AUB-C)**

High quality evidence demonstrates that approximately 13% of women with HMB have biochemically detectable systemic disorders of haemostasis, most often von Willebrand disease. A structured approach to history taking as shown in Table 4 will identify 90% of women with systemic disorders of haemostasis.

*[Insert Table 4]*

HMB may occur with the use of anticoagulant drugs such as warfarin, heparin, and low molecular weight heparin. There is impairment of the formation of an adequate “plug” or clot within the vascular lumen. Originally the FIGO MDC determined that this type of iatrogenic AUB should be placed in the AUB-C category. The 2018 update of the FIGO, PALM-COEIN classification system has moved AUB associated with anticoagulation into the category “AUB-I”.

### **Ovulatory dysfunction (AUB-O)**

Ovulatory dysfunction (anovulation) is often secondary to other disorders resulting in hormonal fluctuations such as polycystic ovary syndrome, hypothyroidism, hyperprolactinemia, mental stress, obesity, anorexia, weight loss, or extreme exercise. Ovulatory dysfunction frequently occurs at the extremes of reproductive age: adolescence and the menopause. In some instances, hormonal fluctuations may be iatrogenic, caused by sex steroids or drugs that impact dopamine metabolism. The 2018 update of the FIGO, PALM-COEIN classification system recommends that therapies interfering with the H-P-O axis and are associated with AUB, now be placed in the “AUB-I” category.

### **Endometrial (AUB-E)**

AUB that occurs in the context of a structurally normal uterus with regular menstrual cycles in the absence of a coagulopathy is likely to represent a primary endometrial disorder of the mechanisms regulating local endometrial haemostasis. Tests measuring such abnormalities are not currently available.

### **Iatrogenic (AUB-I)**

Unscheduled endometrial bleeding that occurs during the use of sex steroid therapy is termed “breakthrough bleeding (BTB)” and is a major component of this classification. It is likely that many episodes of unscheduled bleeding or BTB are related to reduced circulating hormone levels, secondary to compliance issues such as missed, delayed, or erratic use, use of anticonvulsants and antibiotics (e.g. rifampin and griseofulvin) and cigarette smoking. This may reduce levels of contraceptive steroids because of enhanced hepatic metabolism. Many women experience unscheduled vaginal spotting or bleeding in the first 3–6 months of use of the levonorgestrel-releasing intrauterine system (LNG-IUS) and should be appropriately counselled. Indeed, all progestin-only contraceptive methods are associated with episodes of unscheduled bleeding in 20% of users and all women should be counselled about this side effect.

Tricyclic antidepressants (e.g. amitriptyline and nortriptyline) and phenothiazines impact dopamine metabolism by reducing serotonin uptake and result in reduced inhibition of prolactin release. This may result in anovulation and consequent AUB. As noted above, AUB associated with anticoagulant use, is now also included in this category as per the 2018 FIGO, PALM-COEIN classification update.

**Not “yet” classified [AUB-N; revised in 2018 to not “otherwise” classified]**

Entities such as chronic endometritis, arteriovenous malformations; or bleeding from a caesarean section scar defect or isthmocoele may be associated with or contribute to AUB/HMB.

## **MANAGEMENT APPROACH TO AUB**

A structured history and other associated symptoms can indicate a potential underlying cause of AUB. These may represent structural causes (AUB-L, AUB-P, AUB-A), iatrogenic AUB (AUB-I), and disorders of ovulation (AUB-O). AUB-M should always be considered especially in women with a raised BMI, diabetes, hypertension, PCOS, age >45 years, nulliparity, late menopause, unopposed oestrogen exposure, tamoxifen use, family history of breast, colon, endometrial cancer e.g. Lynch syndrome or other risk factors for endometrial cancer. As mentioned earlier, AUB-C may also be diagnosed with a targeted history. Table 5 summarises an appropriate history in women presenting with AUB.

*[Insert Table 5]*

## **INVESTIGATION IN AUB/HMB**

Table 6 summarises the investigations in women with HMB/AUB as per current NICE guidance.

*[Insert Table 6]*

## **Management of AUB/HMB**

Management of women with AUB/HMB is complex with an interplay of several factors.

This may include conservative treatment (a period of observation), medical or surgical treatment (excisional and non-excisional therapies), depending on the patient's age, parity, cause of bleeding, co-existing morbidities, the desire for fertility preservation, impact on the quality of life and patient preference.

### *Nonpharmacological management*

A careful explanation of the cause of AUB is essential and exclusion of pathology will often allay fears and provide reassurance, such that women may simply choose to monitor their menstrual cycles using a menstrual calendar. Monitoring is made easy with the abundance of “apps” available on modern smart devices for this purpose.

Regular exercise and maintenance of a healthy body mass index (BMI) should be recommended as a higher BMI is often associated with AUB-O. Exercise and a healthy diet will also help limit iron deficiency anaemia, raise energy levels and improve quality of life.

### *Pharmacological management*

Flow chart A, provides a simplified approach to women presenting with AUB/HMB and Table 7 provides a summary of the commonly used pharmacological methods used in treating women with AUB/HMB.

*[Insert Table 7]*

## **FIBROIDS AND AUB/HMB**

An extremely common cause of AUB/HMB are fibroids (myomas, leiomyomas). Uterine fibroids are the most common benign tumours in women of reproductive age. Although hysterectomy offers a permanent solution to the complaint of AUB/HMB, a significant proportion of symptomatic fibroids are seen in younger women who desire uterine and/or fertility preservation and hence medical treatments have an important role to play.

Probably the most important medical therapy for management of fibroids in recent years are the selective progesterone receptor modulators (SPRMs). These SPRMs impart a tissue-specific partial progesterone antagonist effect and act upon progesterone receptors in the endometrium and the underlying myometrial tissue. Ulipristal acetate (UPA) is the only SPRM specifically approved and commercialised to date for management of symptomatic uterine fibroids. UPA controls HMB in over 90% of women, with an overall decrease in bleeding similar to GnRH agonist use but has a faster onset of amenorrhea usually within 10 days. Oestradiol levels are maintained in the mid-follicular phase range during treatment thereby reducing the menopausal symptoms. UPA does cause the benign endometrial changes described as PAEC (progesterone receptor modulator associated endometrial changes). These changes are reversible after treatment discontinuation.

UPA use was placed under review in February 2018 by the European Medicines Agency (EMA) and the Medicines and Healthcare Products Regulatory Agency (MHRA) due to eight reports of serious liver injury, including cases of hepatic failure requiring liver transplantation, reported in Europe in women using UPA for uterine fibroids. The up-to-date MHRA guidance in August 2018 following completion of the EMA review is available here - <https://www.gov.uk/drug-safety-update/esmya-ulipristal-acetate-and-risk-of-serious-liver->

[injury-new-restrictions-to-use-and-requirements-for-liver-function-monitoring-before-during-and-after-treatment](#)

Restricted indications and new contraindications for UPA use (August 2018) in the United Kingdom are summarised in Table 8. Vilaprisan is a newer SPRM, currently under investigation.

*[Insert Table 8]*

## **NON-EXCISIONAL TREATMENT FOR AUB/HMB**

Endometrial ablation (second-generation) and transcervical resection of the endometrium (TCRE), represent non-excisional methods of treating AUB/HMB and offer an alternative to hysterectomy in women who have no desire for fertility preservation. Both procedures are effective, and satisfaction rates are high. Although hysterectomy is associated with longer operating, a longer recovery period and higher rates of postoperative complications, it offers permanent relief from heavy menstrual bleeding.

Non-excisional treatment for fibroids include; Uterine Artery Embolisation (UAE). Magnetic Resonance Imaging guided High Frequency Ultrasound (MRgFUS), Radiofrequency Volumetric Thermal Ablation (RFVTA), Laparoscopic or Vaginal Uterine Artery Ligation Laparoscopic thermomyolysis and Laparoscopic Cryomyolysis.

## **SURGICAL TREATMENT FOR AUB/HMB**

It is beyond the scope of this article to discussion surgical treatments for individual causes of AUB/HMB (PALM – structural causes), but a brief summary is presented below in Table 9.

*[Insert Table 9]*

## **CONCLUSION**

AUB is common and negatively impacts the quality of life of women worldwide and has clinical implications and high costs for the healthcare systems. The PALM-COEIN acronym maybe be used as a foundation of care; it improves the understanding of the causes of AUB, and in doing so facilitates effective history taking, examination, investigations and onward management. A range of treatment options are available, which should be tailored to the woman's individual need and the desire for uterine/fertility preservation, to reduced treatment failures, improve satisfaction rates and avoid the need for major excisional surgery.

## **CONFLICT OF INTEREST**

Rohan Chodankar is supported as a Clinical Research Fellow by Bayer AG and has no other conflict of interest. HODC has clinical research support for laboratory consumables and staff from Bayer AG and provides consultancy advice (but with no personal remuneration) for Bayer AG, PregLem SA, Gedeon Richter, Vifor Pharma UK Ltd, AbbVie Inc., Myovant Sciences GmbH. HODC receives royalties from UpToDate for article on abnormal uterine bleeding.

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**FURTHER READING: (no more than 5 important sources)**

Munro MG, Critchley HOD, Fraser IS, Committee FMD. The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. *Int J Gynaecol Obstet*. 2018; 143: 393-408

NICE. NG88: Heavy Menstrual Bleeding: assessment and management National Institute for Health and Clinical Excellence (NICE); 2018. Available from: <https://www.nice.org.uk/guidance/ng88>.

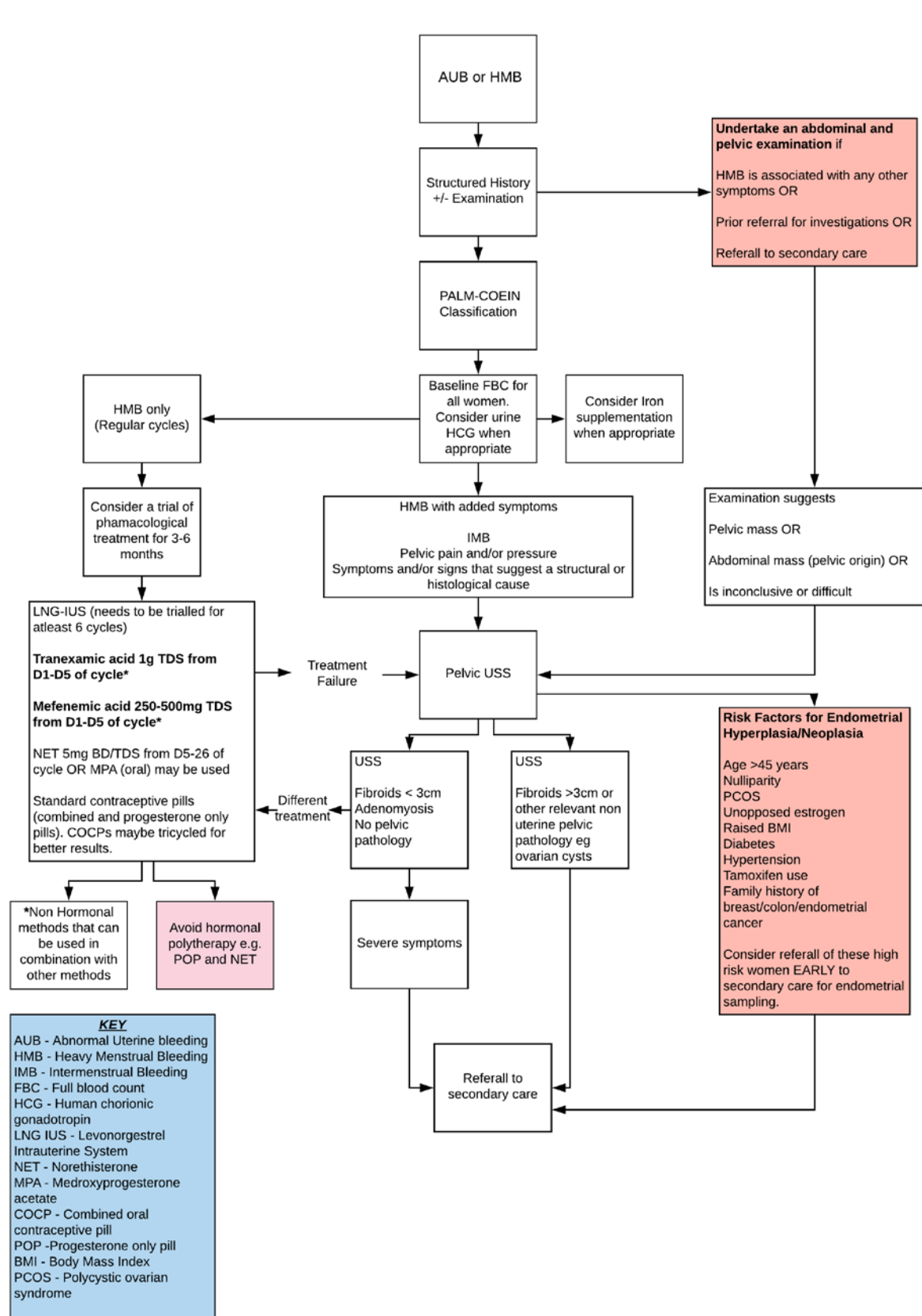
Kouides PA, Conard J, Peyvandi F, Lukes A, Kadir R. Hemostasis and menstruation: appropriate investigation for underlying disorders of hemostasis in women with excessive menstrual bleeding. *Fertil Steril*. 2005; 84: 1345-1351.

RCOG. National Heavy Menstrual Bleeding Audit - Final Report. London: RCOG; 2014. Available from: [https://www.rcog.org.uk/globalassets/documents/guidelines/research--audit/national\\_hmb\\_audit\\_final\\_report\\_july\\_2014.pdf](https://www.rcog.org.uk/globalassets/documents/guidelines/research--audit/national_hmb_audit_final_report_july_2014.pdf);

Maybin JA, Critchley HO. Menstrual physiology: implications for endometrial pathology and beyond. *Hum Reprod Update*. 2015; 21: 748-761;



## MANAGEMENT OF AUB/HMB – CHART A



Risk factors for endometrial hyperplasia and neoplasia have been adapted from the RCOG

(<https://www.rcog.org.uk/globalassets/documents/guidelines/research--audit/advice-for-hmb-services-booklet.pdf>)

## TABLES

**Table 1 – Parameters of the Normal Menstrual Cycle [Adapted from Munro et al, Int J Gynaecol Obstet 2018]**

Parameter	Normal Limits (5 <sup>th</sup> to 95 <sup>th</sup> centile)
Frequency of menses (days)	24 to 38 days
Regularity (Cycle length)	$\leq 7$ to 9 days Cycle length is the number of days from the first day of one menstrual cycle to the first day of the next. No more than seven to nine days difference between the shortest to longest cycles
Duration (days of bleeding in a single menstrual period)	$\leq 8$ days
Volume (monthly blood loss)	Clinical definition is subjective and defined as a volume of menstrual blood loss that does not interfere with a woman's physical, social, emotional, and/or quality of life

**Table 2 - AUB Terminology Cycle [Adapted from Munro et al, Int J Gynaecol Obstet 2018]**

<b><u>Parameters</u></b>	<b><u>Terminology</u></b>	<b><u>Out with 5th to 95th centile</u></b>
Frequency of menses (days)	Absent	Amenorrhoea – Primary or Secondary
	Infrequent	>38 days
	Frequent	<24 days
Regularity (Cycle length)	Irregular	Shortest to longest cycle variation ≥ 10 days
Duration (days of bleeding in a single menstrual period)	Prolonged	> 8 days
Volume (monthly blood loss)	Heavy or light	Subjectively defined

**Table 3 – Abandoned Terminology**

Menorrhagia
Metrorrhagia
Dysfunctional Uterine Bleeding (DUB)
Epimenorrhea and Epimenorrhagia
Hypomenorrhea and Hypermenorrhea
Polymenorrhea and Polymenorrhagia
Menometrorrhagia
Oligomenorrhea

**Table 4 – Identifying women with AUB-C [Adapted from Kouides et al, Fertil Steril 2005]**

Structured history—positive screen if
(a) Excessive menstrual bleeding since menarche, or
(b) History of one of the following—postpartum haemorrhage, surgery-related bleeding, or bleeding associated with dental work, or
(c) History of two or more of the following— bruising greater than 5 cm once or twice/ month, epistaxis once or twice/month, frequent gum bleeding, family history of bleeding symptoms.

**Table 5 – Appropriate history in women with AUB**

<b>HISTORY IN WOMEN WITH AUB</b>		
<u>Menstrual History</u> <ul style="list-style-type: none"> <li>• Menstrual calendar (frequency, duration, volume, regularity)</li> <li>• Duration of HMB/AUB symptoms</li> <li>• Impact on the quality of life (QoL)</li> <li>• Intermenstrual bleeding</li> <li>• Postcoital Bleeding</li> <li>• Age at menarche (if relevant)</li> </ul>	<u>Associated Symptoms</u> <ul style="list-style-type: none"> <li>• Pain during periods (dysmenorrhea)</li> <li>• Chronic pelvic pain</li> <li>• Abnormal vaginal discharge</li> <li>• Pressure symptoms (constipation, urinary frequency)</li> </ul>	<u>Sexual and Reproductive History</u> <ul style="list-style-type: none"> <li>• Parity and mode of birth</li> <li>• Need for fertility preservation</li> <li>• Need for contraception</li> <li>• Sexually transmitted infections (STIs)</li> <li>• Cervical smear history</li> </ul>
<u>Personal History</u> <ul style="list-style-type: none"> <li>• Smoking</li> <li>• Alcohol</li> <li>• Systemic disorders</li> <li>• Drug history (pharmacological and recreational)</li> <li>• Occupation</li> <li>• Recent weight gain or loss</li> <li>• Coagulopathy screen (Table 4)</li> </ul>	<u>Family history</u> <ul style="list-style-type: none"> <li>• Venous Thromboembolic events (VTE)</li> <li>• Cancer</li> <li>• Disorders of haemostasis</li> </ul>	

**Table 6 – Investigations in women with AUB as per NICE guidance.**

<b>INVESTIGATIONS FOR WOMEN WITH AUB/HMB</b>		
<b>TYPE</b>	<b>SPECIFIC TEST</b>	<b>INDICATION</b>
Blood tests	Full Blood Count	Baseline testing to exclude anaemia
	Thyroid profile	In women with symptoms of thyroid disease
	Coagulation Screen	In women who have HMB since the onset of their periods or those with personal or family history suggestive of a coagulation disorder.
	Female Hormone profile	Do not perform routinely
	Serum Ferritin	Do not perform routinely
Histology	Endometrial Sampling	Rule out endometrial hyperplasia and or cancer.  NICE (2018) proposes blind endometrial sampling should be avoided and performed in the context of hysteroscopy.
Imaging	Ultrasound	Ultrasound (transvaginal) is the preferred method to rule out structural abnormalities e.g. fibroids, adenomyosis. If unacceptable, transabdominal ultrasound or magnetic resonance imaging (MRI) should be organised.
	Hysteroscopy	NICE (2018) suggests women should be offered vaginoscopically performed outpatient hysteroscopy in a “see and treat” setting, if their history suggests submucosal fibroids, polyps or endometrial pathology as a first line investigation.

**Table 7 – Pharmacological management of AUB**

Therapy	Evidence for use
Tranexamic Acid (TXA)	40% to 50% reduction in MBL per cycle. Antifibrinolytic treatment is better at improving MBL than other medical treatments, except for the levonorgestrel-releasing intrauterine system (LNG-IUS). No evidence that side effects (including life-threatening blood clots) is increased compared to placebo or other treatments for HMB. TXA is particularly useful in women who either desire pregnancy immediately or for whom hormonal treatment is inappropriate. The drug is cost-effective and improves health-related quality of life.
Non-steroidal anti-inflammatory drugs (NSAIDs)	Benefits are modest; although MBL is reduced, a proportion of women will still have objective HMB. Gastrointestinal effects, are less likely with mefenamic acid compared to other NSAIDs. Efficacy of NSAIDs is superseded by tranexamic acid and LNG IUS. Beneficial in women where dysmenorrhea is present with AUB/HMB.
Levonorgestrel-releasing intrauterine system (LNG-IUS)	Significant reduction in MBL from baseline in HMB in women, including selected women with fibroids as compared to standard oral treatments. More effective than oral medical therapies and results in better quality of life outcomes (QoL). Not as effective as hysterectomy in reducing MBL but improvements in QoL were similar. The role of the LNG-IUS as a treatment for HMB in primary care settings versus other medical treatments was demonstrated by the ECLIPSE study.
Cyclical Progestogens (e.g. Medroxyprogesterone acetate or Norethisterone)	Progestogens administered from day 15 or 19 to day 26 of the cycle offer no advantage over other medical therapies. Progestogen therapy for 21 days (day 5-26) of the cycle results in a significant reduction in menstrual blood loss (up to 80%), although less acceptable choice than LNG-IUS.
Combined Oral Contraceptive Pill (COCP)	COCP can provide cycle control and reduce menstrual blood loss (up to 50%), but there are not enough data to determine its value in comparison with other drugs. The COCP may be used in a triphasic or tricycling manner to reduce the number of menstrual



	<p>bleeds to 3-4 per year. UKMEC criteria may be used to assess suitability (<a href="http://www.fsrh.org/ukmec/">http://www.fsrh.org/ukmec/</a>).</p>
<p>Injectable progestogen, e.g. depot medroxyprogesterone acetate</p>	<p>Intramuscular or subcutaneous injection of high dose progestogens (e.g., depot medroxyprogesterone acetate [DMPA]) can induce amenorrhea in up to 50% of users.</p> <p>Women may have a transient but reversible reduction in their bone mineral density with long-term use.</p>
<p>Gonadotropin-releasing hormone agonists (IM, SC or intranasal) ± add- back</p>	<p>Excellent efficacy, with an amenorrhea rate of up to 90%. However, they are associated with very significant menopausal side effects secondary to oestrogen deficiency that limit routine or ad hoc use. Limitation of these side effects can be achieved with 'add-back' hormone replacement therapy (HRT, e.g. Tibolone) usually introduced after 6 months of use.</p>
<p>Progesterone only pill (POP or Minipill)</p>	<p>POP is associated with irregular and unpredictable blood loss and it is not usually recommended as a primary treatment for AUB, unless other treatments have failed or are contraindicated. Desogestrel containing POPs may provide effective treatment in some women.</p>
<p>Problem specific treatments</p>	<p>It is beyond the scope of this article to discuss treatments for individual causes of AUB/HMB, e.g. AUB-C managed using DDVAP and/or Tranexamic acid.</p>
<p>Acute AUB (non gestational)</p>	<p>Although high quality evidence is limited in this group of women, both COCP and medroxyprogesterone acetate have similar efficacy.</p>

**Table 8 - Restricted indications and new contraindications for UPA use (August 2018) in the United Kingdom**

<u>Indications</u>	<u>Liver function monitoring</u>
<ul style="list-style-type: none"> <li>• UPA is indicated for the intermittent treatment of moderate to severe symptoms of uterine fibroids in women of reproductive age who are not eligible for surgery</li> <li>• UPA is indicated for one course of pre-operative treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age</li> <li>• UPA treatment is to be initiated and supervised by a physician experienced in the diagnosis and treatment of uterine fibroids</li> <li>• UPA is contraindicated in women with underlying liver disorders</li> </ul>	<ul style="list-style-type: none"> <li>• Before initiation of each treatment course: perform liver function tests; do not initiate UPA in women with baseline alanine transaminase (ALT) or aspartate aminotransferase (AST) more than 2-times the upper limit of normal [ULN]</li> <li>• During the first 2 UPA treatment courses: perform liver function tests every month.</li> <li>• For further treatment courses: perform liver function tests once before each new course and when clinically indicated.</li> <li>• At the end of each treatment course: perform liver function tests after 2–4 weeks. Stop UPA treatment and closely monitor women with ALT or AST more than 3-times upper limit of normal; consider the need for specialist hepatology referral.</li> </ul>

**Table 9 – Surgical management of AUB**

<b><u>Causes of AUB/HMB</u></b>	<b><u>Surgical Treatment</u></b>
Polyp	Avulsion (usually cervical polyps) Hysteroscopic resection or removal
Adenomyosis	Adenomyomectomy Hysterectomy
Leiomyoma (Fibroids)	Myomectomy Hysterectomy Consider pre-treatment with GnRH analogues or SPRMs
Malignancy	Often a combination of radical excisional surgery +/-radiotherapy+/- chemotherapy or palliative surgery.

## **SBA QUESTIONS**

A 46-year-old woman presents to the Gynaecology Clinic after treatment with 4 courses of Ulipristal acetate (UPA), which was commenced for heavy menstrual bleeding in association with a fibroid uterus. She completed her last course 1 week ago and is yet to have a menstrual bleed. Her ultrasound scan today suggests a reduction in the uterine size and fibroid size. Her endometrial thickness is 16 mm. She has been amenorrhoeic on the UPA treatment and feels well today. Which of the following statements is true?

- A. She may be offered another course of UPA after her 1 menstrual bleed
- B. She can be offered another course of UPA after her 2 menstrual bleeds
- C. She should be offered immediate endometrial sampling
- D. She should be offered immediate liver function tests
- E. She should be offered liver function tests in 2-4 weeks of completing UPA course

Answer:

Correct answer is E. Option D is false.

UPA is currently licensed for use for 4 courses. So, options A and B are false.

Benign endometrial thickening is known with UPA use – PAEC or Progesterone Receptor

Modulator Associated Endometrial change. These changes are reversible upon

discontinuation of UPA. In This patient should be rescanned after a menstrual bleed. If the

endometrial thickness is MORE than 16 mm, endometrial sampling should be offered. Option

C is hence false.

A 30-year para 1 with a BMI of 24, fit and well presents to the Gynaecology Clinic with abnormal uterine bleeding. She describes an irregular cycle to no pattern over the last 12 months. Her cervical smear and STI screening tests are normal. Her pelvic ultrasound reveals a structurally normal uterus with a endometrial thickness of 4 mm with normal ovaries. She had a etonogestrel subdermal implant inserted 20 months ago for contraception after the birth of her child. She has been trialled on the mini pill, combined pill, tranexamic acid, norethisterone with no benefit. She is at the end of her tether and requests an ablation or hysterectomy. This is a difficult decision as her family isn't complete. She has had an eating disorder as a child and does not wish any treatments that may cause weight gain. Which of the following management choices is best suited?

- A. GnRH analogues
- B. Depot Medroxyprogesterone acetate
- C. Removal of the etonogestrel subdermal implant
- D. Endometrial Biopsy
- E. Endometrial Ablation
- F. Hysterectomy with ovarian conservation

Answer

Correct answer is C, In the first instance this patient should be offered a “hormonal medication” free period as she has been trialled on a polytherapy of hormones with a etonogestrel subdermal implant in situ. This may be responsible for AUB-I. The etonogestrel subdermal implant by itself may be responsible for unscheduled bleeding in up to 20% of users.

Options E and F are not suitable as the patient's family isn't complete.

GnRH analogues are a short-term measure and should not be used ad hoc when the aetiology of AUB is unclear. Option A is incorrect.

Depot Medroxyprogesterone acetate is also a progestin and could contribute to AUB I. Also, DMPA is associated with weight gain. Option B is incorrect.

The patient has no clear indication for endometrial sampling (age, thin ET on USS, normal BMI). Option D is incorrect in the first instance, however may need to be undertaken to further clarify AUB aetiology.